Sel je t’aime

JM Krzesinski

Chef de service de néphrologie

CHU Liège

Apport en sel, de quoi parle-t'on?

L'apport quotidien conseillé est de 2,3 g (2300 mg) de sodium (Na), ce qui vaut environ:

- 5,8 g (5800 mg) de sel (dit aussi chlorure de sodium ou NaCl)ou
- 100 mmoles de l'ion Na^+ ou
- une cuillère à café de sel.

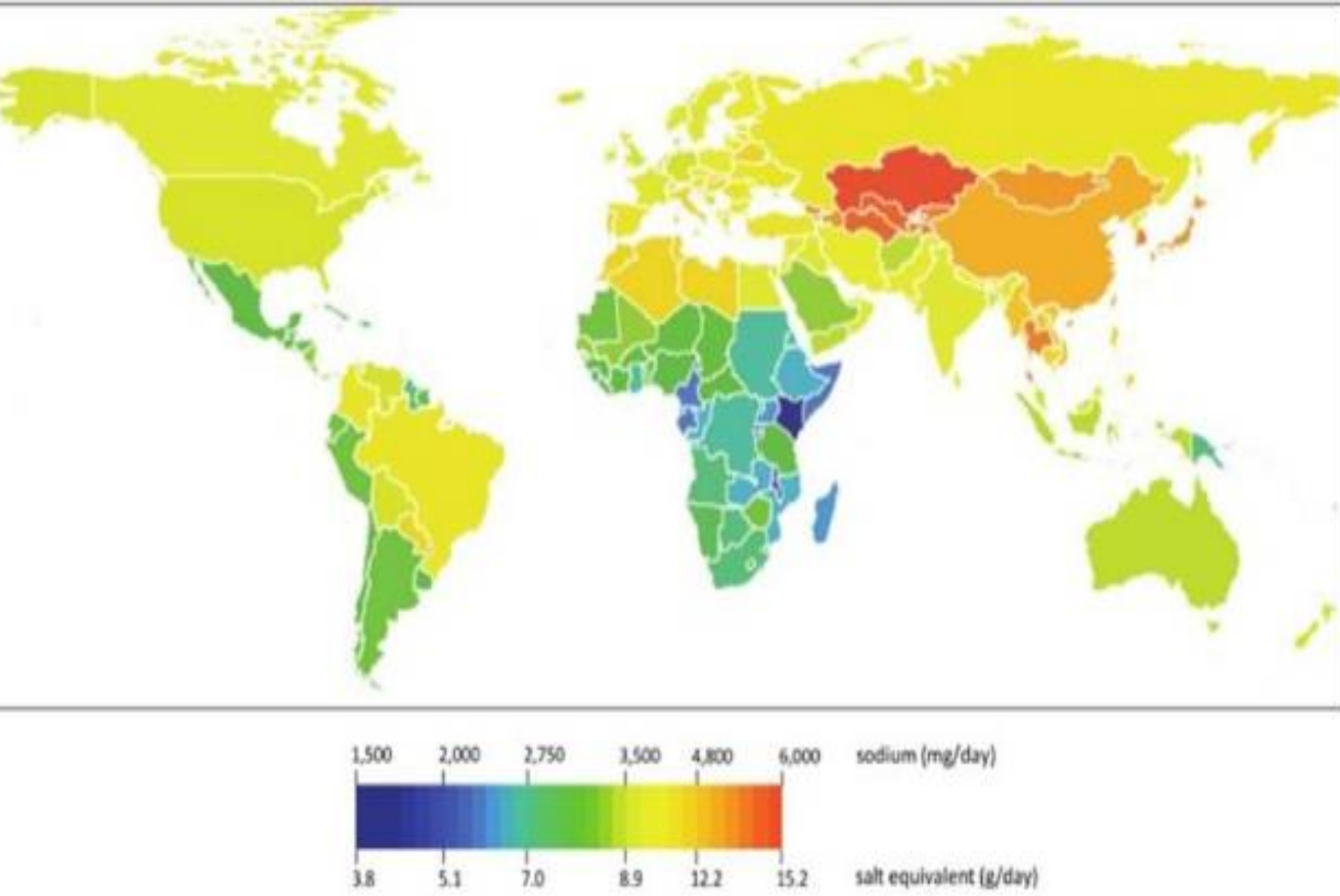
Régulation de la balance sodée

- L'apport quotidien en sodium varie en fait de 30 à 450 mmoles/j (soit de 2 à 25 g de NaCl/j)
- Les pertes sudorales et digestives sont < 20 mmoles/j en conditions normales
- La majorité du sodium est éliminée par les reins.
- La quantification de l'apport sodé s'effectue, le plus précisément, sur base de plusieurs récoltes d'urines de 24h!

Développement d'un intérêt pour le sel

- A l'âge de la pierre: consommation / jour: 700mg
- Depuis 10000 ans, utilisation pour la conservation des aliments (élément stratégique)
- Développement d'un goût et d'un commerce pour le sel (or blanc), symbole d'amitié, de loyauté, d'hospitalité
- A l'époque romaine, consommation quotidienne de 25g (préservation de la santé: salus, salubritas) et utilisation comme salaire (salarium, ration pour le sel)
- Au Moyen-Age, apparition d'une taxe royale sur le sel en France (Gabelle: 6% des revenus royaux). Apparition de la salière.

Au contraire de l'ère ancienne, le sel ne fait pas du tout défaut dans l'alimentation d'aujourd'hui!



Mean global sodium intakes in 2010, by country worldwide (from Powles et al., 2013).

Sel et risque cardiovasculaire ?

Figure 1. Salt cellar made of gold, enamel, and ebony by Benvenuto Cellini (1500 to 1571) and presented in 1543 as gift to Francois I, King of France (1494 to 1547). The salt cellar, valued at approximately US $55 million, was stolen in May 2003 from the Kunsthistorisches Museum, Vienna, Austria. It was recovered undamaged by the Austrian police in January 2006. (Photograph obtained from unrestricted web page of FBI Top Ten Art crimes. Available at: http://www.fbi.gov/hq/cid/arttheft/topten/cellini.htm. Accessed April 11, 2007.)

Rôle du sel dans la genèse de l'HTA

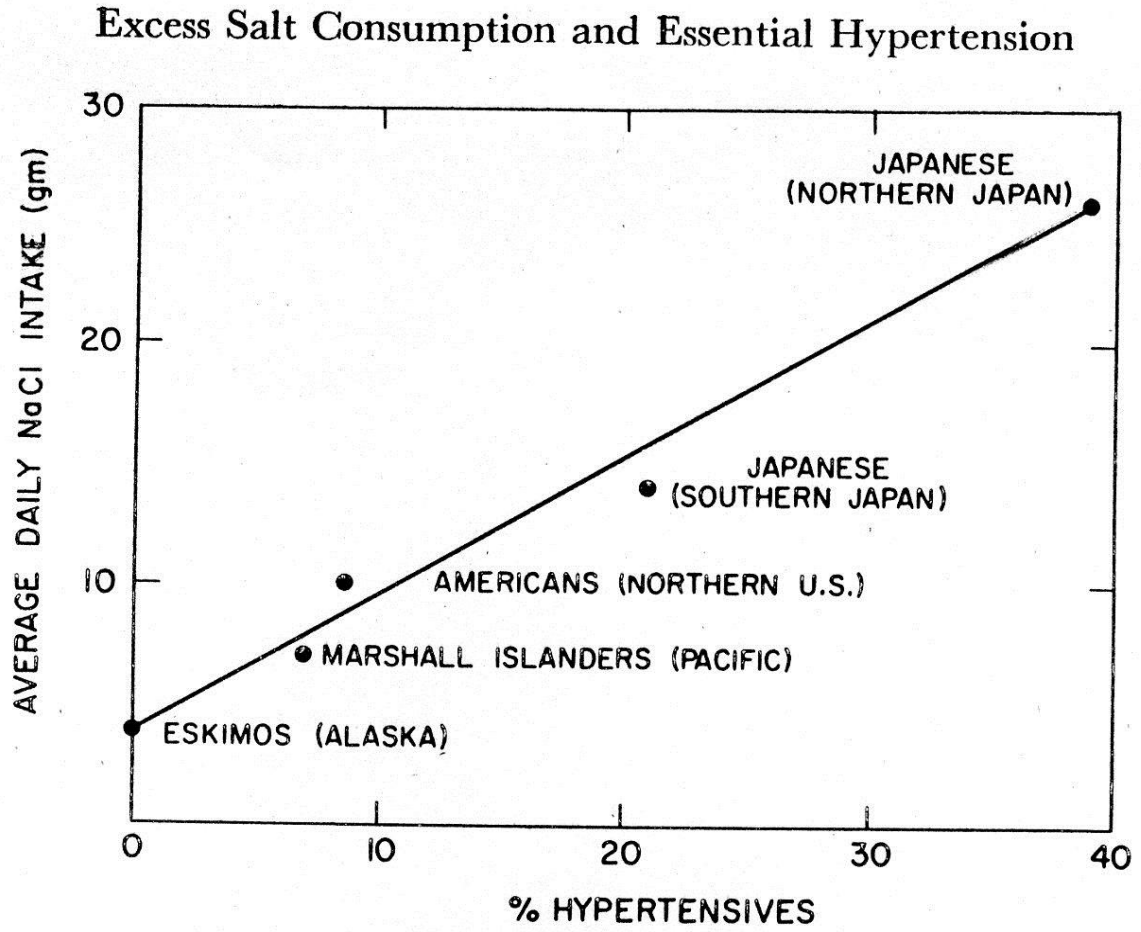


FIG. 1. Correlation of average daily salt (NaCl) intakes with prevalence of hypertension in different geographic areas and among different races. FROM: DAHL, L. K. In: Essential Hypertension. An International Symposium. Berlin, 1960. Springer-Verlag.

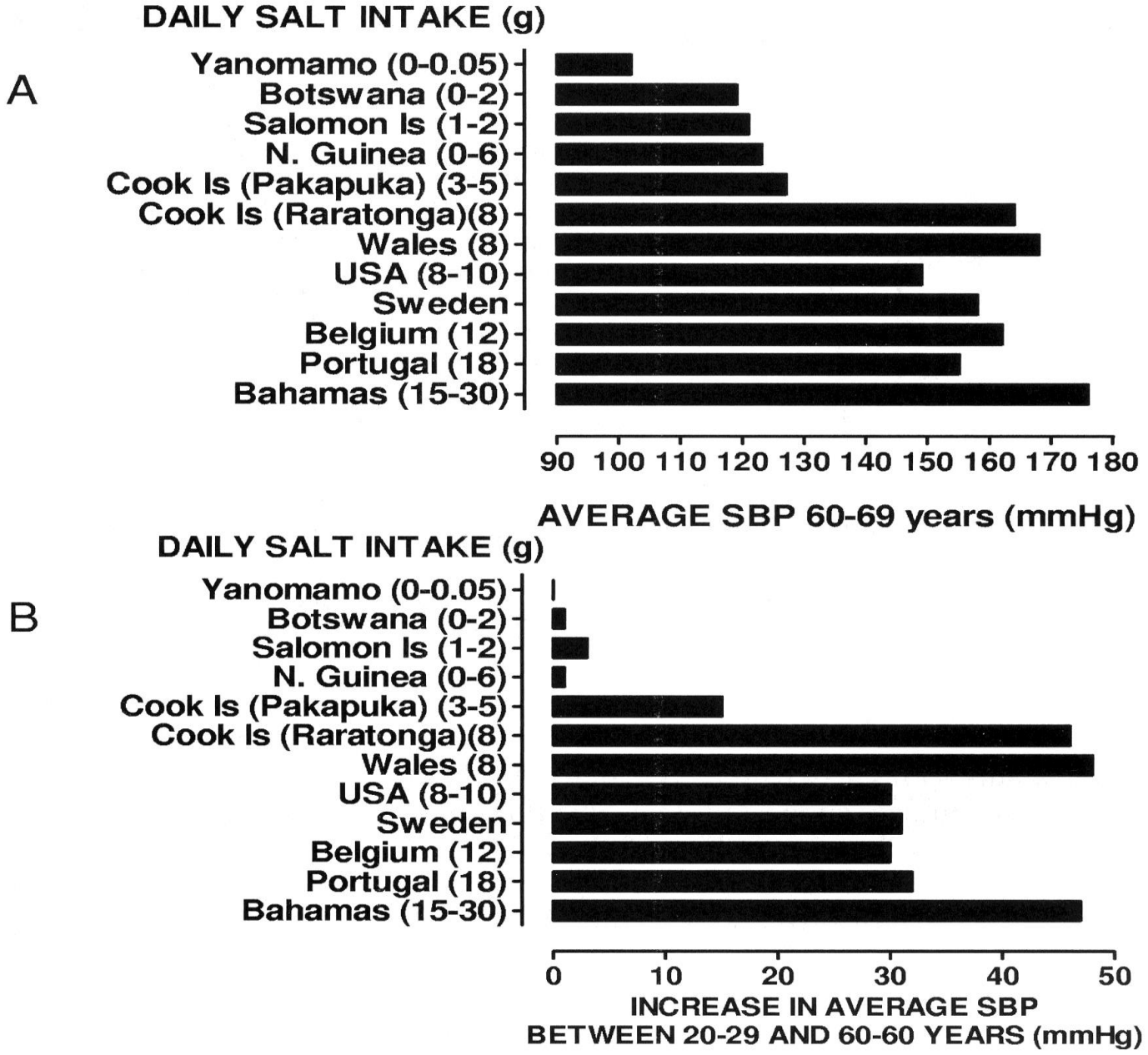


Figure 2. (A) Habitual daily salt intake and average systolic blood pressure (SBP) in selected populations 60 to 69 years old and (B) the difference in average SBPs at 20 to 29 years of age in the corresponding populations. More than 80% of hypertensive patients older than 60 years have salt sensitivity.[42] (Data adapted from Meneton et al,[11] who quoted Joosens JV: Dietary salt restriction: The case in favor. R Soc Med Ser 26:243-250, 1980.)

INTERSALT
6 g/d more salt during 30y ⟶
Rise in BP of 10/6 mmHg

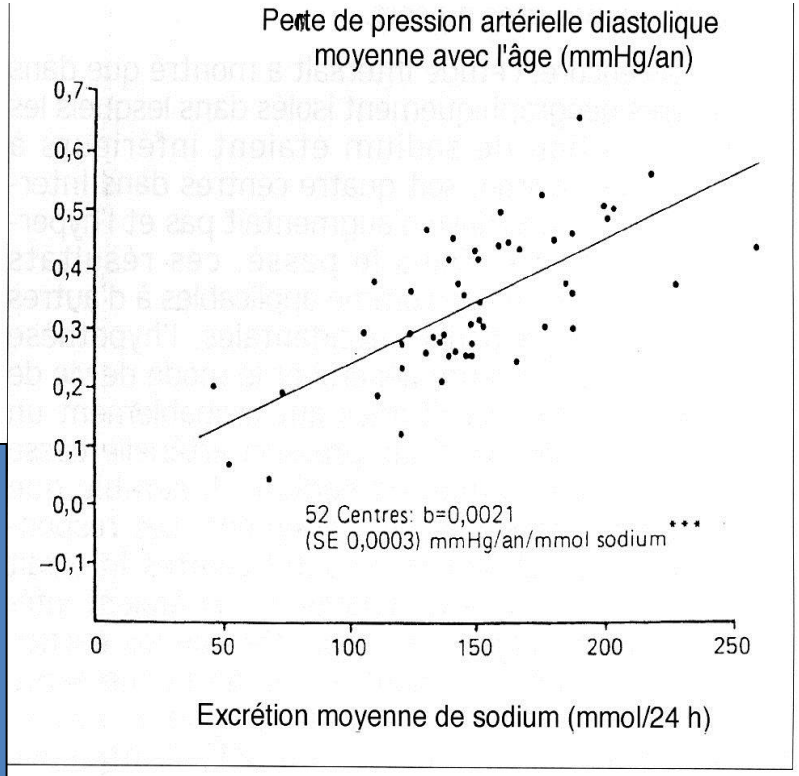


FIG. 5 - Graphes transcentre de la pente de la pression artérielle diastolique avec l'âge, et l'excrétion moyenne de sodium et les droites de régression filtrées ajustées pour l'âge, le sexe, l'indice de masse corporelle et la consommation d'alcool dans 52 centres. Extrait de : Intersalt Cooperative Research Group. Intersalt : An international study of electrolyte excretion and blood pressure. Results for 24-hour urinary sodium and potassium excretions. Br Med J 1988 ; 297 : 319-28.

FIG. 5 - Cross-centre plots of diastolic blood pressure slope with age, and median sodium excretion and filtered regression lines standardized for age, sex, body mass index and alcohol consumption for 52 centres. From : Intersalt Cooperative Research Group. Intersalt : An international study of electrolyte excretion and blood pressure. Results for 24-hour urinary sodium and potassium excretions. Br Med J 1988 ; 297 : 319-28.

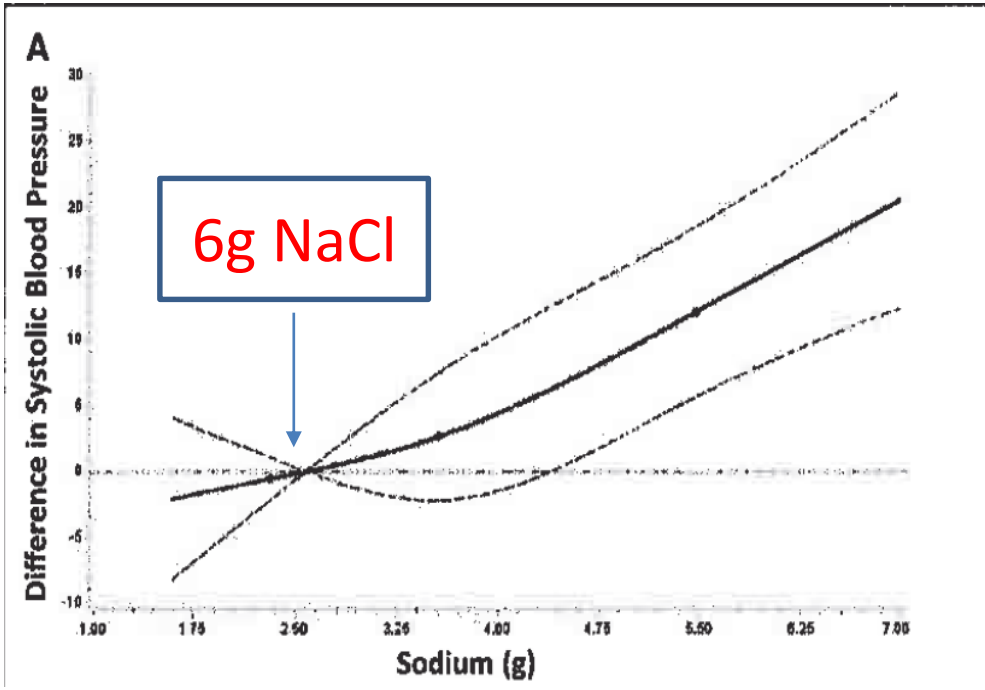
LIÈGE université Médecine

Association Between Urinary Sodium and Potassium Excretion and Blood Pressure Among Adults in the United States

Circulation. 2018;137:237–246.

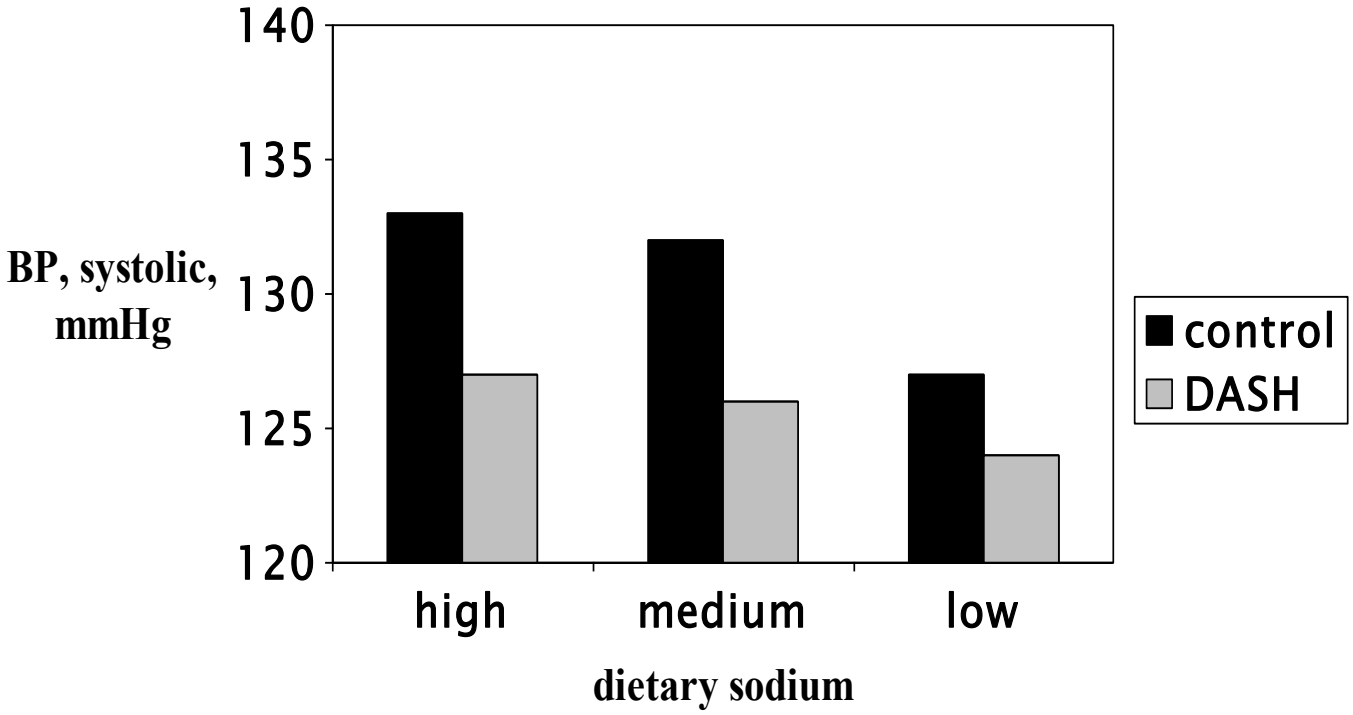
National Health and Nutrition Examination Survey, 2014

METHODS: Cross-sectional data were obtained from 766 participants age 20 to 69 years with complete blood pressure and 24-hour urine collections in the 2014 National Health and Nutrition Examination Survey, a nationally representative survey of the US noninstitutionalized population. Usual 24-hour urinary electrolyte excretion (sodium, potassium, and their ratio) was estimated from ≤2 collections on nonconsecutive days, adjusting for day-to-day variability in excretion. Outcomes included systolic and diastolic blood pressure from the average of 3 measures and hypertension status, based on average blood pressure ≥140/90 and antihypertensive medication use.



A, The y axis shows the difference in systolic blood pressure across sodium excretion values in comparison with a reference value of 2.58 g (the midpoint of the lowest quartile). The overall association was significant ($P<0.001$)

Effect of different sodium intakes on BP (Sacks et al NEJM 2001)



Relationship between salt restriction and BP

He FJ, MacGregor GA - *The Cochrane Library*, 2007, Issue 2, 1-41.

Figure 01. Relationship between the net change in urinary sodium excretion and systolic blood pressure. The open circles represent normotensives and the solid circles represent hypertensives. The slope is weighted by the inverse of the variance of the net change in systolic blood pressure. The size of the circle is in proportion to the weight of the trial.

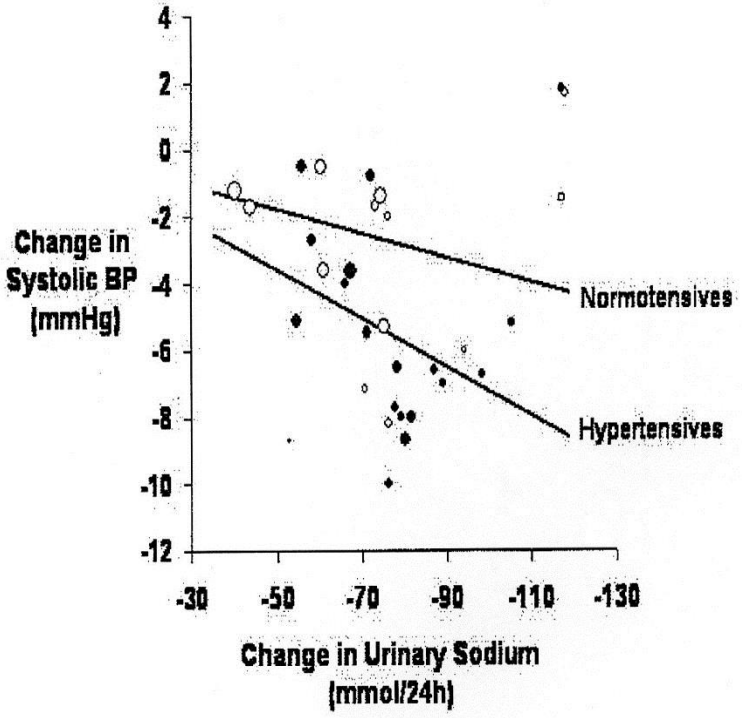
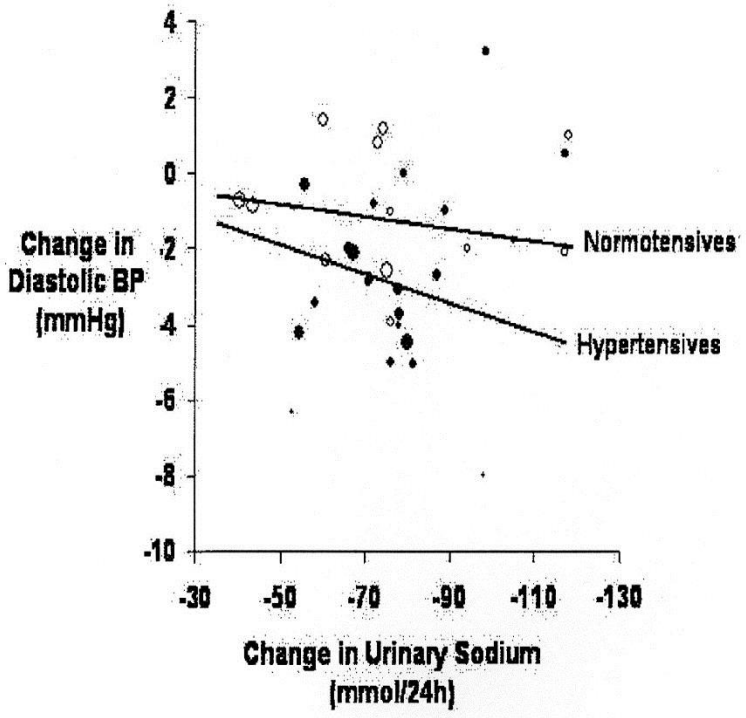


Figure 02. Relationship between the net change in urinary sodium excretion and diastolic blood pressure. The open circles represent normotensives and the solid circles represent hypertensives. The slope is weighted by the inverse of the variance of the net change in diastolic blood pressure. The size of the circle is in proportion to the weight of the trial.



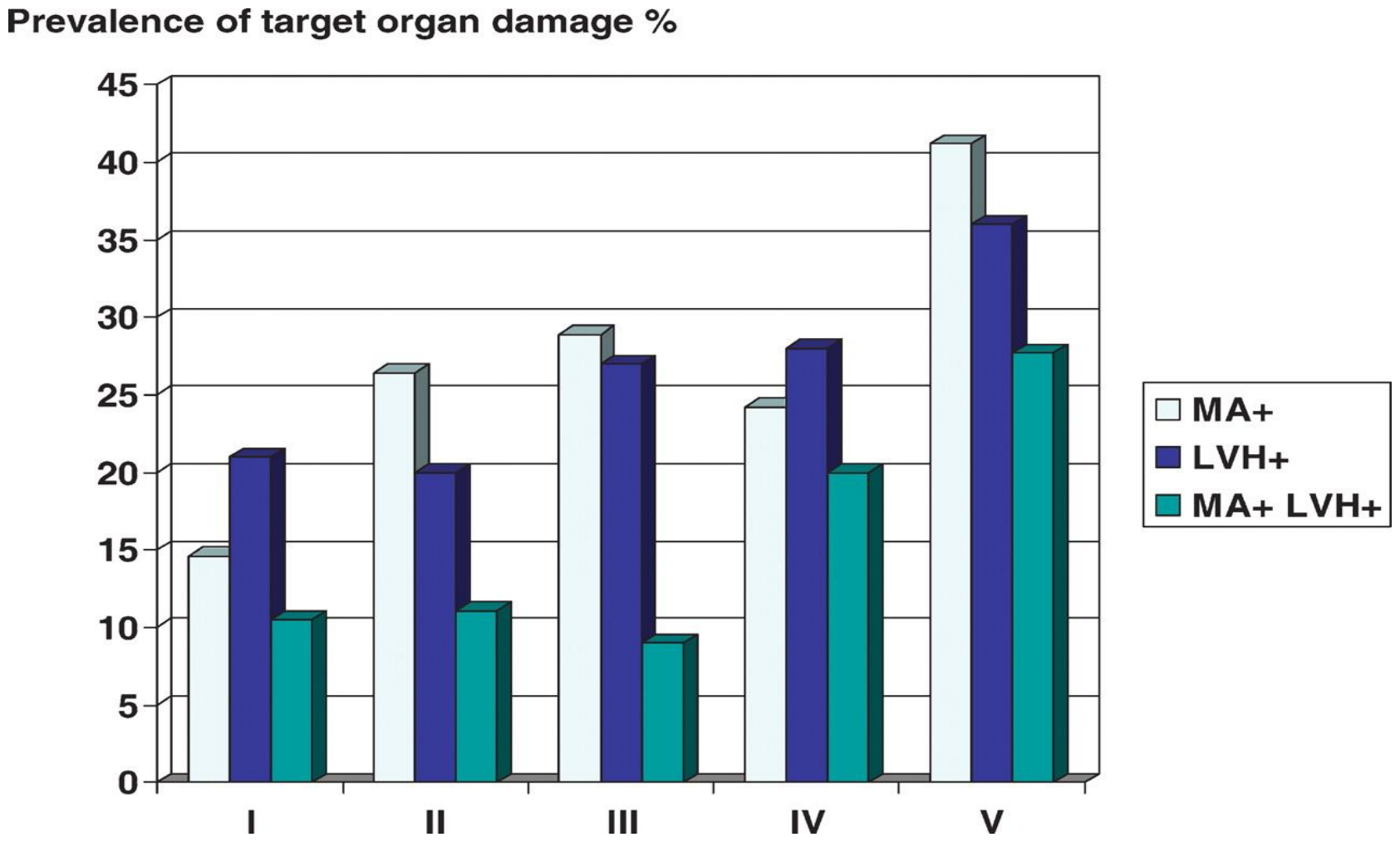
LIÈGE université Médecine

Main results of the meta-analysis of studies about the effect of low NaCl diet on BP

- 34 trials (3230 participants), > 4 weeks duration
- Mean change in uNa : -75 mmol/24h (- 4.4 g Salt)
- Mean change in BP: - 4.2 mmHg SBP (CI -5.1 to -3.2)
  - 2.1 mmHg DBP (CI -2.7 to -1.4)
- In HT, - 5.4 mmHg for SBP/ -2.8 mmHg for DBP
- In NT, -2.4/-1 mmHg

En moyenne 1g NaCl en moins = - 1mmHg de PAS
mais > si Salt Sensitivity: race, âge, sévérité HTA, IRC,..

Prevalence of left ventricular hypertrophy, microalbuminuria or both (MA+ LVH+) according to quintiles of 24-h natriuresis in 450 patients with never-treated essential hypertension aged>= 40 years



Mimran, A. et al. Nephrol. Dial. Transplant. 2008 23:2138-2141; doi:10.1093/ndt/gfn160

Néphropathie diabétique

Curr Opin Nephrol Hypertens 2014, 23:533–540

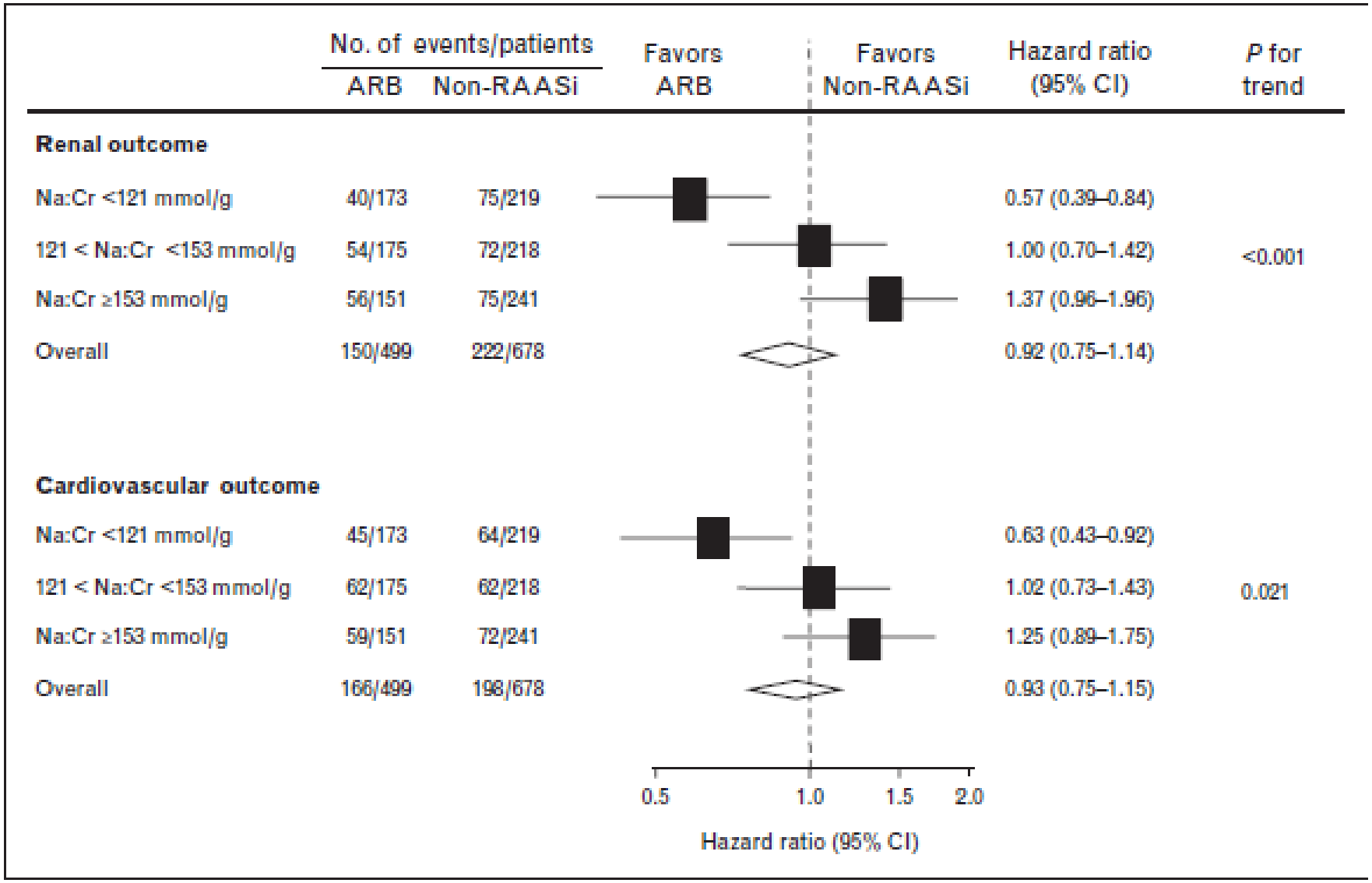


FIGURE 3. Effect of sodium intake by tertile of urinary Na/creatinine (Cr) on the treatment benefit of ARB for renal (upper panels) and cardiovascular (lower panels) outcome in patients with type 2 diabetes and nephropathy. Urinary sodium excretion in the subsequent tertiles corresponded to a dietary salt intake of 8.9, 10.9, and 12.2 g, respectively. ARB,

Vascular effects of dietary salt

Curr Opin Nephrol Hypertens 2015, 24:8–13

David G. Edwards and William B. Farquhar

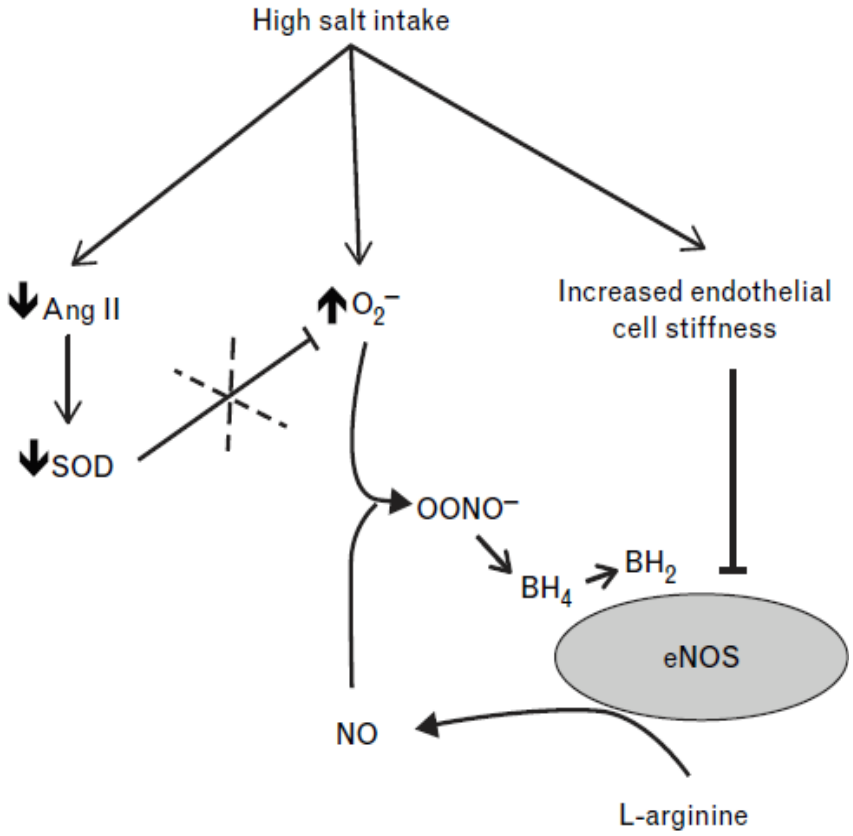


FIGURE 1. Proposed mechanisms by which high salt intake leads to reduced nitric oxide (NO) bioavailability. High salt leads to increased superoxide (O_2^-) production and suppression of angiotensin II (Ang II), which leads to decreased superoxide dismutase (SOD) expression and activity reducing scavenging of O_2^-. NO bioavailability is decreased by the following: via reaction of NO with O_2^- to form peroxynitrite ($OONO^-$); by oxidation of endothelial nitric oxide synthase (eNOS) cofactor tetrahydrobiopterin (BH_4) reducing NO synthesis; and an increase in endothelial cell stiffness which leads to decreased synthesis of NO.

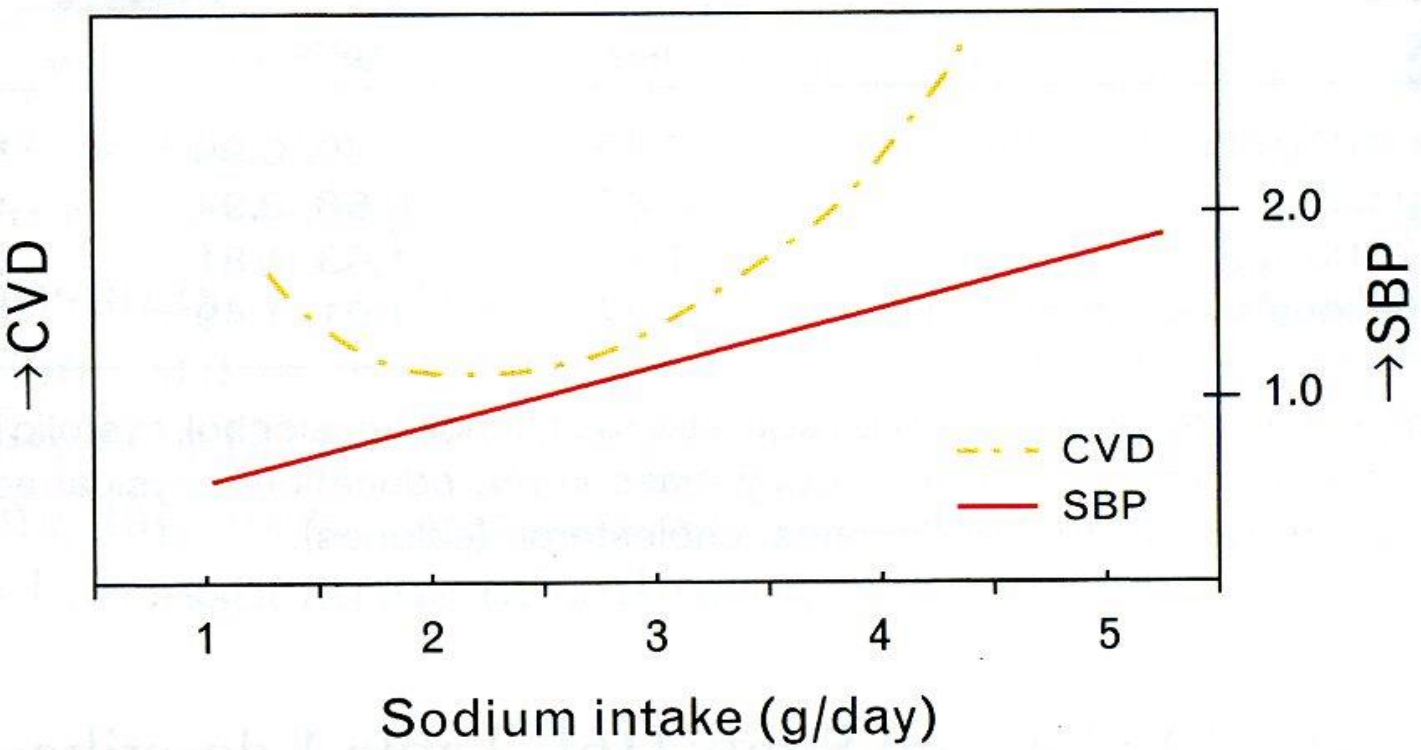
High dietary salt results in impaired endothelial function and increased arterial stiffness, both predictors of cardiovascular disease, independent of changes in blood pressure.

J Am Coll Cardiol. 2013 January 22; 61(3): 335–343. doi:10.1016/j.jacc.2012.09.010.

Dietary sodium restriction reverses vascular endothelial dysfunction in middle-aged/older adults with moderately elevated systolic blood pressure

Kristen L. Jablonski, Ph.D.[*], **Matthew L. Racine, M.S.**[*], **Candace J. Geolfos, B.A.**[*], **Phillip E. Gates, Ph.D.**[†], **Michel Chonchol, M.D.**[‡], **Matthew B. McQueen, Sc.D.**[*], and **Douglas R. Seals,**

Conclusions—DSR largely reverses both macro- and microvascular endothelial dysfunction by enhancing NO and BH_4 bioavailability and reducing oxidative stress. Our findings support the emerging concept that DSR induces "vascular protection" beyond that attributable to its BP-lowering effects.



The relation of dietary sodium intake to systolic blood pressure (SBP) and cardiovascular events (CVD). In normotensive persons a decrease in sodium intake of 160 mmol produces a 1.2 mmHg fall in systolic blood pressure.

Alderman M. – J *Hypertens*, 2007, 125, 903-907.

Compared With Usual Sodium Intake, Low- and Excessive-Sodium Diets Are Associated With Increased Mortality: A Meta-Analysis

Niels Graudal,[1] Gesche Jürgens,[2] Bo Baslund,[1] and Michael H. Alderman[3]

BACKGROUND
The effect of sodium intake on population health remains controversial. The objective was to investigate the incidence of all-cause mortality (ACM) and cardiovascular disease events (CVDEs) in populations exposed to dietary intakes of low sodium (<115 mmol), usual sodium (low usual sodium: 115–165 mmol; high usual sodium: 166–215 mmol), and high sodium (>215 mmol).

METHODS
The relationship between individual measures of dietary sodium intake vs. outcome in cohort studies and randomized controlled trials (RCTs) measured as hazard ratios (HRs) were integrated in meta-analyses.

RESULTS
No RCTs in healthy population samples were identified. Data from 23 cohort studies and 2 follow-up studies of RCTs (n = 274,683) showed that the risks of ACM and CVDEs were decreased in usual sodium vs. low sodium intake (ACM: HR = 0.91, 95% confidence interval (CI) = 0.82–0.99; CVDEs: HR = 0.90, 95% CI = 0.82–0.99) and increased in high sodium vs. usual sodium intake (ACM: HR = 1.16, 95% CI = 1.03–1.30; CVDEs: HR = 1.12, 95% CI = 1.02–1.24). In population representative samples adjusted for multiple confounders, the HR for ACM was consistently decreased in usual sodium vs. low sodium intake (HR = 0.86; 95% CI = 0.81–0.92), but not increased in high sodium vs. usual sodium intake (HR = 1.04; 95% CI = 0.91–1.18). Within the usual sodium intake range, the number of events was stable (high usual sodium vs. low usual sodium: HR = 0.98; 95% CI = 0.92–1.03).

CONCLUSIONS
Both low sodium intakes and high sodium intakes are associated with increased mortality, consistent with a U-shaped association between sodium intake and health outcomes.

Keywords: blood pressure; cardiovascular disease; diet; hypertension; meta-analysis; mortality; salt; sodium chloride; stroke.

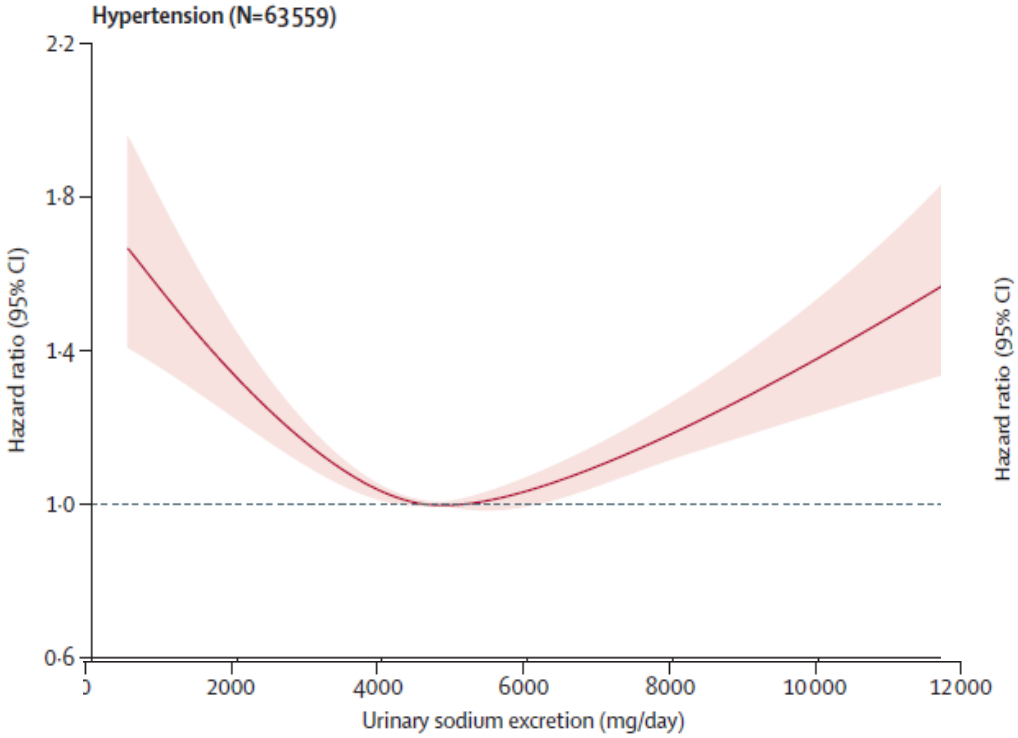
doi:10.1093/ajh/hpu028

Associations of urinary sodium excretion with cardiovascular events in individuals with and without hypertension: a pooled analysis of data from four studies

www.thelancet.com Published online May 20, 2016

Andrew Mente, Martin O'Donnell, Sumathy Rangarajan, Gilles Dagenais, Scott Lear, Matthew McQueen, Rafael Diaz, Alvaro Avezum, Patricio Lopez-Jaramillo, Fernando Lanas, Wei Li, Yin Lu, Sun Yi, Lei Rensheng, Romaina Iqbal, Prem Mony, Rita Yusuf, Khalid Yusoff, Andrzej Szuba, Aytekin Oguz, Annika Rosengren, Ahmad Bahonar, Afzalhussein Yusufali, Aletta Elisabeth Schutte, Jephat Chifamba, Johannes F E Mann, Sonia S Anand, Koon Teo, S Yusuf, for the PURE, EPIDREAM, and ONTARGET/TRANSCEND Investigators

Interpretation Compared with moderate sodium intake, high sodium intake is associated with an increased risk of cardiovascular events and death in hypertensive populations (no association in normotensive population), while the association of low sodium intake with increased risk of cardiovascular events and death is observed in those with or without hypertension. These data suggest that lowering sodium intake is best targeted at populations with hypertension who consume high sodium diets.



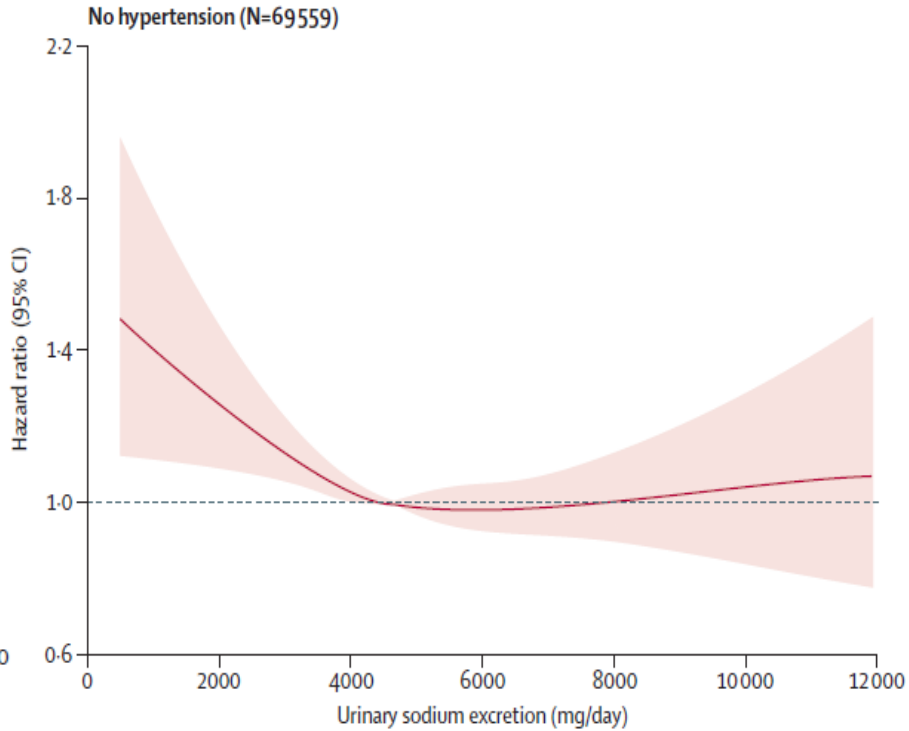


TABLE 2 | Favorable versus unfavorable effects of reduced dietary sodium intake.

Favorable effects	Unfavorable effects
↓ Blood pressure	↑ Cholesterol
↓ Left ventricular hypertrophy	↑ Catecholamines
↑ Antiproteinuric effect of drugs for albuminuria	↑ Renin–angiotensin–aldosterone system activation
↓ Pro-inflammatory state	

Urinary sodium excretion and cardiovascular mortality in Finland: a prospective study

Lancet 2001; **357:** 848–51

Jaakko Tuomilehto, Pekka Jousilahti, Daiva Rastenyte, Vladislav Moltchanov, Antti Tanskanen, Pirjo Pietinen, Aulikki Nissinen

Methods We prospectively followed 1173 Finnish men and 1263 women aged 25–64 years with complete data on 24 h urinary sodium excretion and cardiovascular risk factors. The endpoints were an incident coronary and stroke event, and death from coronary heart disease, cardiovascular disease, and any cause. Each endpoint was analysed separately with the Cox proportional hazards model.

Findings The hazards ratios for coronary heart disease, cardiovascular disease, and all-cause mortality, associated with a 100 mmol increase in 24 h urinary sodium excretion, were 1·51 (95% CI 1·14–2·00), 1·45 (1·14–1·84), and 1·26 (1·06–1·50), respectively, in both men and women. The frequency of acute coronary events, but not acute stroke events, rose significantly with increasing sodium excretion.

Cause of death	Hazard ratio (95%CI)*	Hazard ratio (95% CI)†
Men (n=1173)		
Coronary heart disease (n=54)	1·45 (1·07–1·97)	1·55 (1·12–2·13)
Cardiovascular (n=72)	1·43 (1·10–1·86)	1·38 (1·04–1·82)
All causes (n=136)	1·33 (1·09–1·61)	1·30 (1·06–1·59)
Women (n=1263)		
Coronary heart disease (n=7)	1·96 (0·92–4·17)	2·07 (0·80–5·36)
Cardiovascular (n=15)	1·55 (0·84–2·84)	1·43 (0·73–2·78)
All causes (n=44)	0·99 (0·64–1·54)	0·91 (0·56–1·47)
Men and women together‡ (n=2436)		
Coronary heart disease (n=61)	1·51 (1·14–2·00)	1·56 (1·15–2·12)
Cardiovascular (n=87)	1·45 (1·14–1·84)	1·36 (1,05–1·76)
All causes (n=180)	1·26 (1·06–1·50)	1·22 (1·02–1·47)

Hazard ratios associated with a 100 mmol increase in 24 h sodium intake.
*Adjusted for age and study year.
†Adjusted for age, study year, smoking, serum total and HDL cholesterol, systolic blood pressure, and body mass index.
‡Adjusted also for sex.

Table 2: **Hazards ratios of coronary heart disease, cardiovascular, and all-cause mortality associated with 24 h urinary sodium excretion**

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VOL. 68, NO. 15, 2016

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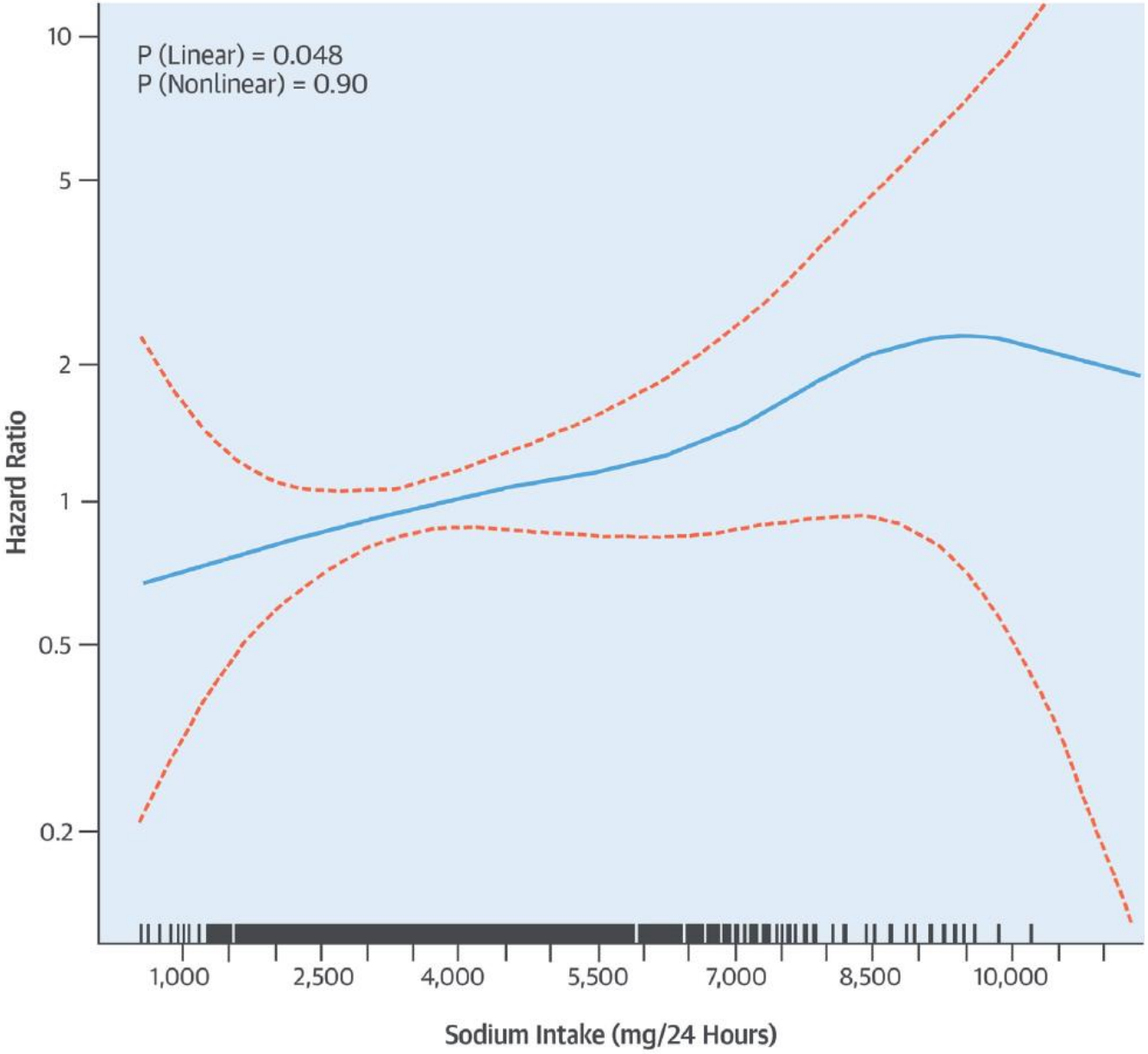
http://dx.doi.org/10.1016/j.jacc.2016.07.745

ORIGINAL INVESTIGATIONS

Sodium Intake and All-Cause Mortality Over 20 Years in the Trials of Hypertension Prevention

Nancy R. Cook, ScD,[a] Lawrence J. Appel, MD,[b] Paul K. Whelton, MD[c]

CENTRAL ILLUSTRATION Sodium and All-Cause Mortality Over 20 Years



Cook, N.R. et al. J Am Coll Cardiol. 2016;68(15):1609-17.

LIÈGE université Médecine

Dietary Sodium and Cardiovascular Disease Risk — Measurement Matters

Mary E. Cogswell, Dr.P.H., Kristy Mugavero, M.S.N., M.P.H., Barbara A. Bowman, Ph.D., and Thomas R. Frieden, M.D., M.P.H.

N Engl J Med. 2016 August 11; 375(6): 580–586.

Dietary Sodium Content, Mortality, and Risk for Cardiovascular Events in Older Adults

The Health, Aging, and Body Composition (Health ABC) Study

Andreas P. Kalogeropoulos, MD, MPH, PhD; Vasiliki V. Georgiopoulou, MD; Rachel A. Murphy, PhD; Anne B. Newman, MD, MPH; Douglas C. Bauer, MD; Tamara B. Harris, MD, MS; Zhou Yang, MPH, PhD; William B. Applegate, MD, MPH; Stephen B. Kritchevsky, PhD

JAMA Intern Med. doi:10.1001/jamainternmed.2014.6278
Published online January 19, 2015.

DESIGN, SETTING, AND PARTICIPANTS We analyzed 10-year follow-up data from 2642 older adults (age range, 71-80 years) participating in a community-based, prospective cohort study (inception between April 1, 1997, and July 31, 1998).

EXPOSURES Dietary sodium intake at baseline was assessed by a food frequency questionnaire. We examined sodium intake as a continuous variable and as a categorical variable at the following levels: less than 1500 mg/d (291 participants [11.0%]), 1500 to 2300 mg/d (779 participants [29.5%]), and greater than 2300 mg/d (1572 participants [59.5%]).

CONCLUSIONS AND RELEVANCE In older adults, food frequency questionnaire–assessed sodium intake was not associated with 10-year mortality, incident CVD, or incident HF, and consuming greater than 2300 mg/d of sodium was associated with nonsignificantly higher mortality in adjusted models.

Dietary Sodium Content, Mortality, and Risk for Cardiovascular Events in Older Adults

The Health, Aging, and Body Composition (Health ABC) Study

Andreas P. Kalogeropoulos, MD, MPH, PhD; Vasiliki V. Georgiopoulou, MD; Rachel A. Murphy, PhD; Anne B. Newman, MD, MPH; Douglas C. Bauer, MD; Tamara B. Harris, MD, MS; Zhou Yang, MPH, PhD; William B. Applegate, MD, MPH; Stephen B. Kritchevsky, PhD

Figure 2. Ten-Year All-Cause Mortality in the Health ABC Study According to Baseline Dietary Sodium Intake

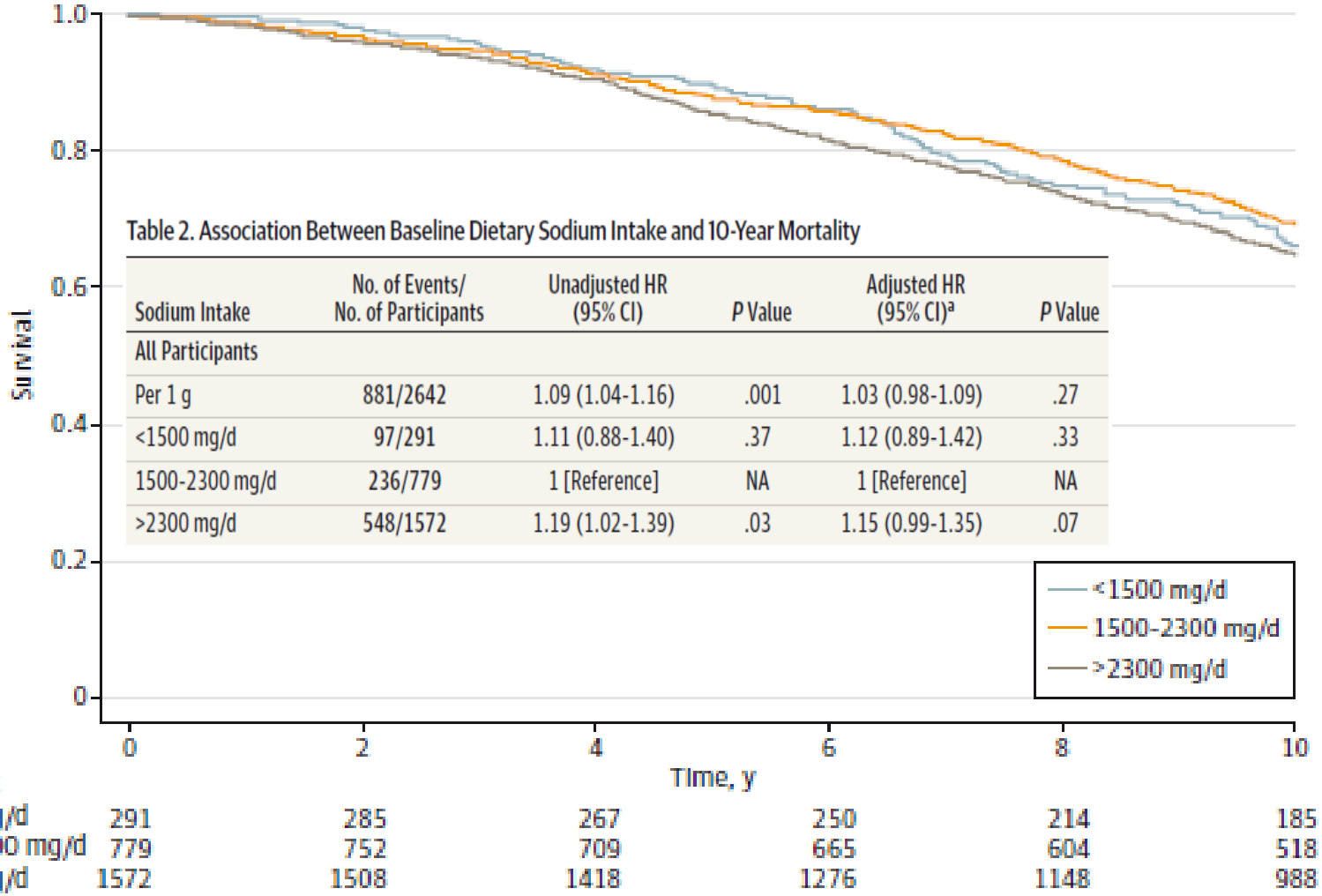


Table 2. Association Between Baseline Dietary Sodium Intake and 10-Year Mortality

Sodium Intake	No. of Events/ No. of Participants	Unadjusted HR (95% CI)	*P* Value	Adjusted HR (95% CI)[a]	*P* Value
All Participants					
Per 1 g	881/2642	1.09 (1.04-1.16)	.001	1.03 (0.98-1.09)	.27
<1500 mg/d	97/291	1.11 (0.88-1.40)	.37	1.12 (0.89-1.42)	.33
1500-2300 mg/d	236/779	1 [Reference]	NA	1 [Reference]	NA
>2300 mg/d	548/1572	1.19 (1.02-1.39)	.03	1.15 (0.99-1.35)	.07

JAMA | Original Investigation

Association Between Dietary Factors and Mortality From Heart Disease, Stroke, and Type 2 Diabetes in the United States

JAMA. 2017;317(9):912-924.

OBJECTIVE To estimate associations of intake of 10 specific dietary factors with mortality due to heart disease, stroke, and type 2 diabetes (cardiometabolic mortality) among US adults.

DESIGN, SETTING, AND PARTICIPANTS A comparative risk assessment model incorporated data and corresponding uncertainty on population demographics and dietary habits from National Health and Nutrition Examination Surveys (1999-2002: n = 8104; 2009-2012: n = 8516); estimated associations of diet and disease from meta-analyses of prospective studies and clinical trials with validity analyses to assess potential bias; and estimated disease-specific national mortality from the National Center for Health Statistics.

EXPOSURES Consumption of 10 foods/nutrients associated with cardiometabolic diseases: fruits, vegetables, nuts/seeds, whole grains, unprocessed red meats, processed meats, sugar-sweetened beverages (SSBs), polyunsaturated fats, seafood omega-3 fats, and sodium.

Proportional cardiometabolic mortality attributable to dietary habits in the United States in 2012

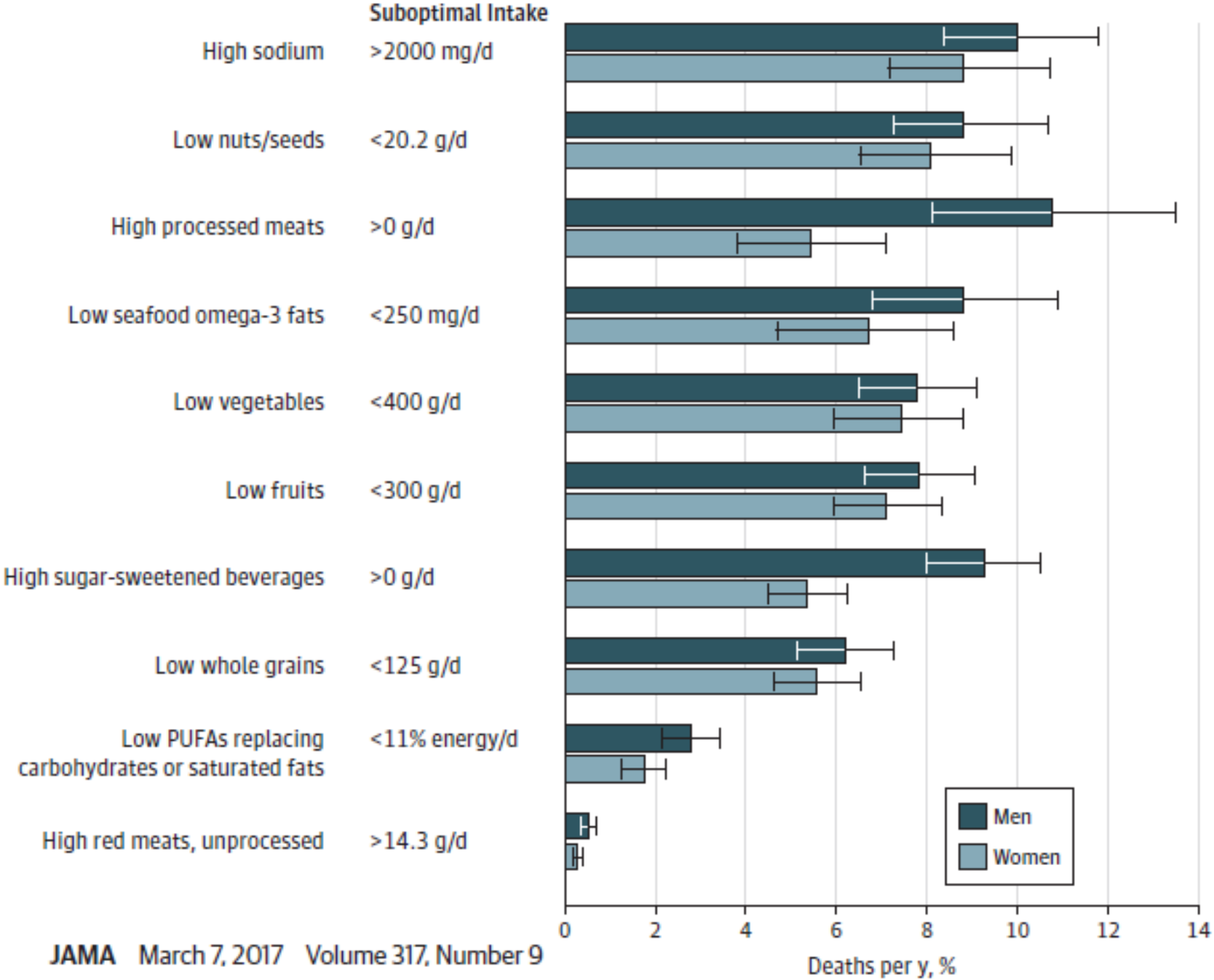
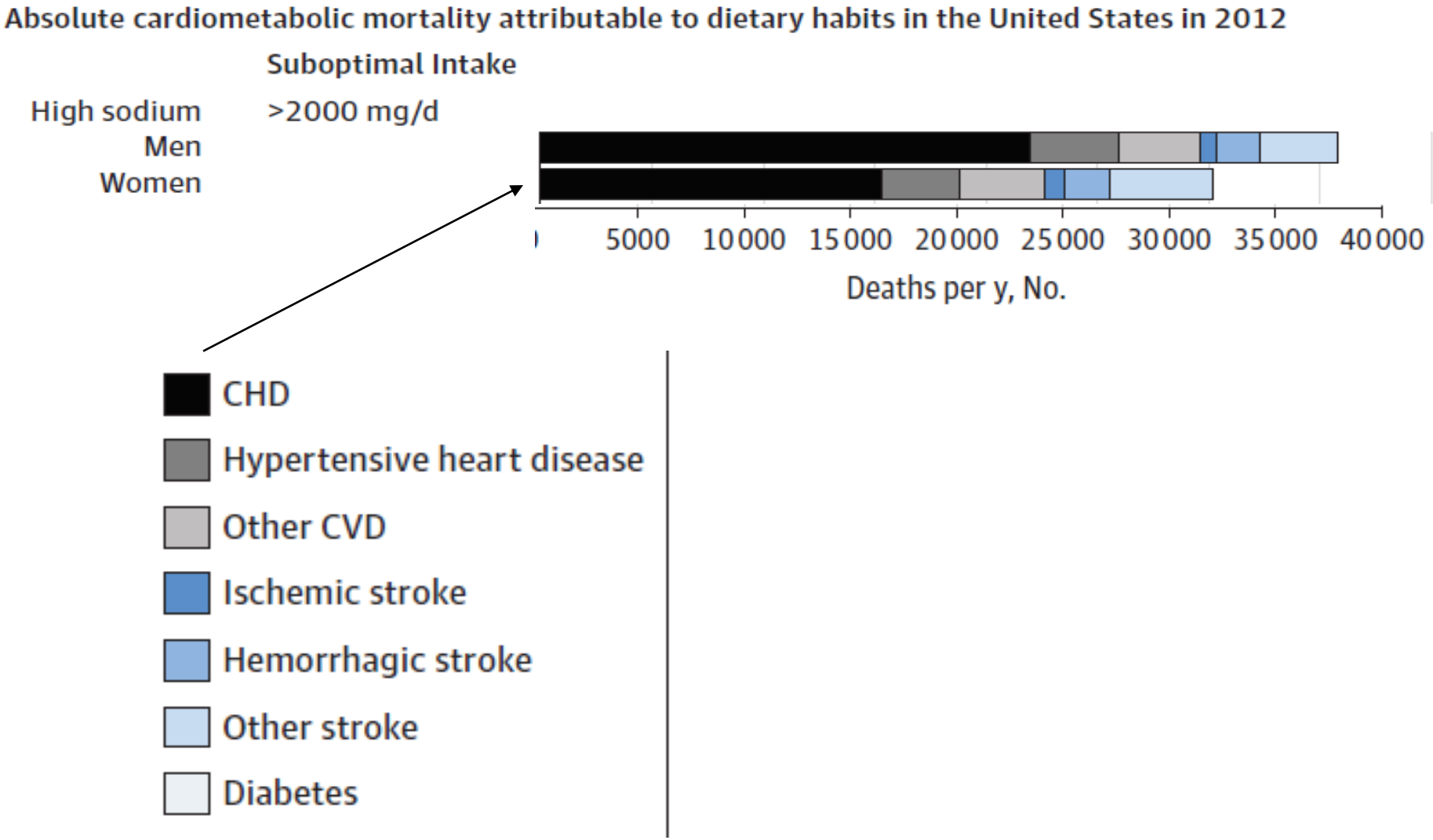


Figure 1. Absolute and Proportional Cardiometabolic Disease Mortality Associated With Suboptimal Dietary Habits Among US Men and Women in 2012

JAMA. 2017;317(9):912-924.



ESC
European Society of Cardiology

European Heart Journal (2018) **00**, 1–98
doi:10.1093/eurheartj/ehy339

Lifestyle interventions for patients with hypertension or high-normal BP

Recommendations	Class[a]	Level[b]
Salt restriction to <5 g per day is recommended.[248,250,255,258]	I	A

2018 American guidelines

Hypertension. 2018:71:1269-1324.

I	A	3. Sodium reduction is recommended for adults with elevated BP or hypertension.[S6-8–S6-12]

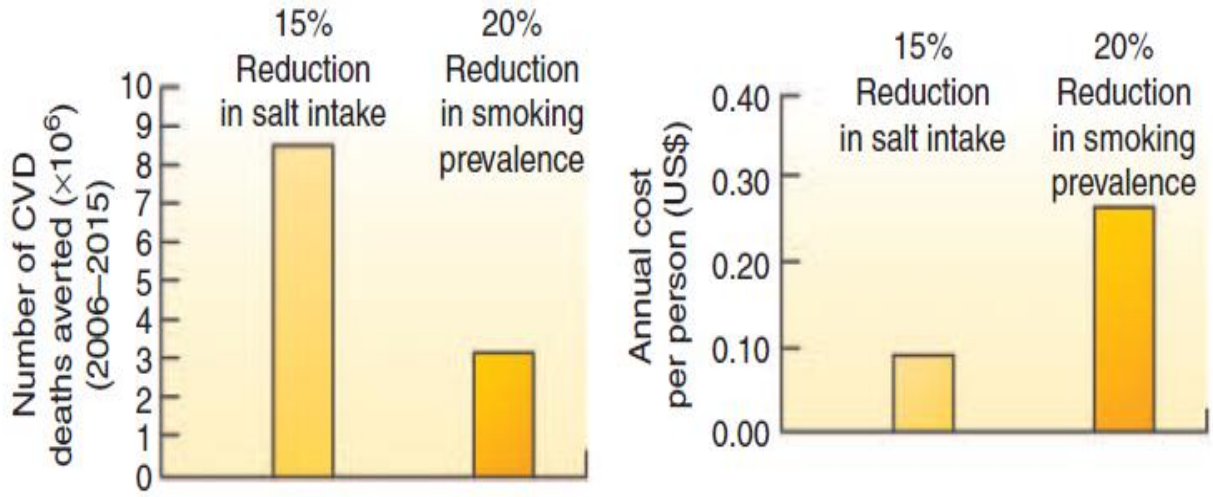


Figure 3 | Number of cardiovascular disease (CVD) deaths averted and the financial costs associated with implementation of salt reduction and tobacco control in 23 low- and middle-income countries. Adapted from Asaria *et al.*[24]

Kidney International (2010) **78,** 745–753;

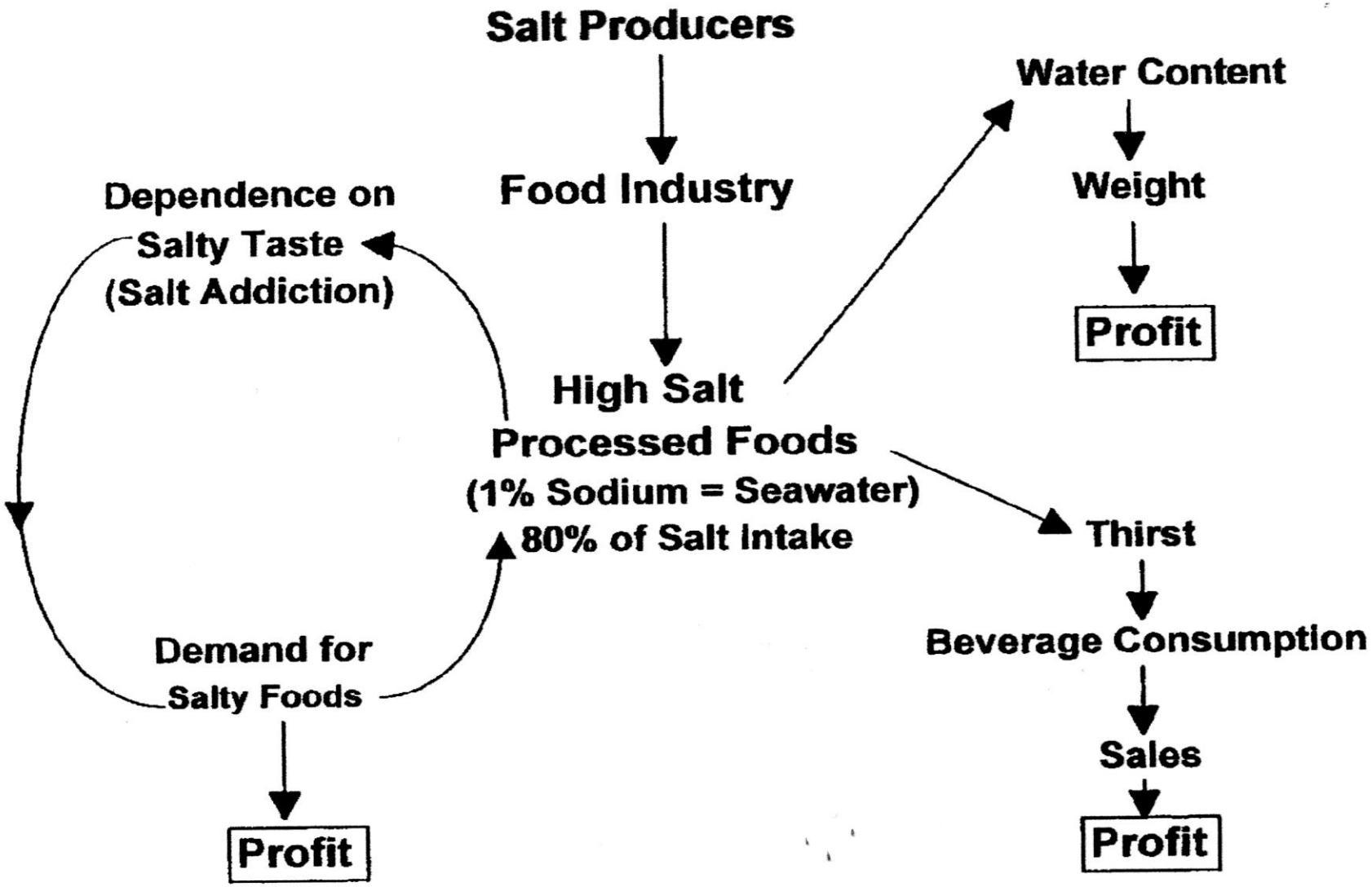


Fig. 5. The commercial importance of salt in processed food.

MacGregor G.A. – *Nephrol Dial Transplant*, **1998**, 13, 2471-2479.

International recommendations: max 6g/d of NaCl in HT
WHO, Guideline: Sodium intake for adults and children 2012

Table 1 | UK strategy for reducing salt

	Salt intake		
Source	g/day	Reduction needed	Target intake (g/day)
Table/cooking (15%)	1.4 g	40% reduction	0.9 g
Natural (5%)	0.5 g	No reduction	0.5 g
Food industry (80%)	7.6 g	40% reduction	4.6 g
	Total: 9.5 g		Target: 6.0 g

Kidney International (2010) **78**, 745–753;

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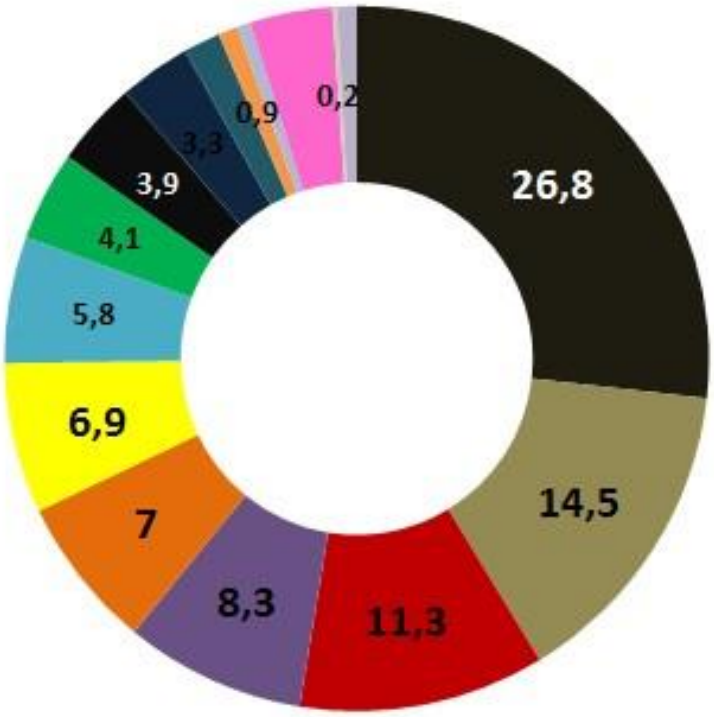
Contributions moyennes des groupes d'aliments (en %) aux apports en sodium chez les adultes

Quoidansmonassiette.fr
Etude INCA2



- Pain, céréales
- Condiments sauces, soupes, bouillons
- Charcuteries
- Plats composés
- Pizza, quiches, sandwichs
- Fromages
- Viennoiseries, biscuits, pâtisseries
- Légumes et légumes secs
- Viande, vollaille, abat, œufs
- Lait, produits laitiers, crèmes desserts
- Boissons, eau
- Chocolat, sucre, café, glace
- Matières grasses
- Poissons, crustacés

¾ apports

Conclusions

- Le sel est indispensable pour plusieurs fonctions vitales mais trop engendre un risque d'HTA et un risque cardiovasculaire.
- Une réduction de la quantité consommée est à imposer (de façon individuelle)mais dans des limites raisonnables.
- Des encouragements répétés sont indispensables.

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Questions?